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phosphatase STEP (Lombroso et al., Proc. Natl. Acad. Sci. USA 88: 7242-7246 (1991)), (4) ezrin-domain containing PTPases: PTPMEG1 (Guet al., Proc. Natl. Acad. Sci. USA 88: 5867-57871 (1991)), PTPH1 (Yang and Tonks, Proc. Natl. Acad. Sci. USA 88: 5949-5953 (1991)), PTPD1 and PTPD2 (Møller et al., Proc. Natl. Acad. Sci. USA 91: 7477-7481 (1994)), FAP-1/BAS (Sato et al., Science 268: 411-415 (1995); Banville et al., J. Biol. Chem. 269: 22320-22327 (1994); Maekawa et al., FEBS Letters 337: 200-206 (1994)), and SH2 domain containing PTPases: PTP1C/SH-PTP1/SHP-1 (Plutzky et al., Proc. Natl. Acad. Sci. USA 89: 1123-1127 (1992); Shen et al., Nature Lond. 352: 736-739 (1991)) and PTP1D/Syp/SH-PTP2/SHP-2 (Vogel et al., Science 259: 1611-1614 (1993); Feng et al., Science 259: 1607-1611 (1993); Bastein et al., Biochem. Biophys. Res. Comm. 196: 124-133 (1993)).

Receptor-type PTPases consist of a) a putative ligand-binding extracellular domain, b) a transmembrane segment, and c) an intracellular catalytic region. The structures and sizes of the putative ligand-binding extracellular domains of receptor-type PTPases are quite divergent. In contrast, the intracellular catalytic regions of receptor-type PTPases are very homologous to each other and to the intracellular PTPases. Most receptor-type PTPases have two tandemly duplicated catalytic PTPase domains.

The first receptor-type PTPases to be identified were (1) CD45/LCA (Ralph, S.J., EMBO J. 6: 1251-1257 (1987)) and (2) LAR (Streuli et al., J. Exp. Med. 168: 1523-1530 (1988)) that were recognized to belong to this class of enzymes based on homology to PTP1B (Charbonneau et al., Proc. Natl. Acad. Sci. USA 86: 5252-5256 (1989)). CD45 is a family of high molecular weight glycoproteins and is one of the most abundant leukocyte cell surface glycoproteins and appears to be exclusively expressed upon cells of the hematopoietic system (Trowbridge and Thomas, Ann. Rev. Immunol. 12: 85-116 (1994)).

The identification of CD45 and LAR as members of the PTPase family was quickly followed by identification and cloning of